



KRIT1 gene

KRIT1, ankyrin repeat containing

Normal Function

The *KRIT1* gene (also known as *CCM1*) provides instructions for making a protein that strengthens the interactions between cells that form blood vessels and limits leakage from the vessels. The KRIT1 protein interacts with a number of other proteins to form a complex that is found in the junctions that connect neighboring cells. As part of this complex, the KRIT1 protein helps turn off (suppress) a signaling molecule known as RhoA-GTPase. This molecule plays a role in regulating the actin cytoskeleton, which is a network of fibers that makes up the cell's structural framework. When turned on, RhoA-GTPase stimulates the formation of actin fibers, which has been linked to weakened junctions between cells and increased leakage from blood vessels.

Health Conditions Related to Genetic Changes

cerebral cavernous malformation

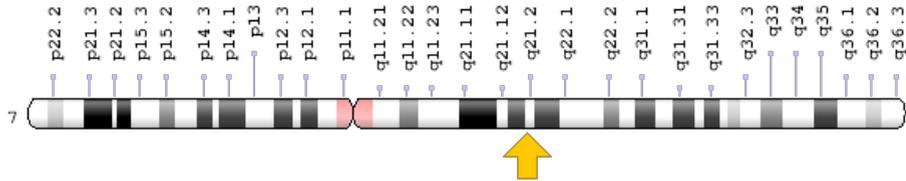
More than 100 *KRIT1* gene mutations have been identified in families with cerebral cavernous malformations, which are collections of blood vessels in the brain that are weak and prone to leakage. Virtually all of these mutations place a premature stop signal in the instructions for making the KRIT1 protein, preventing adequate KRIT1 protein production. A shortage of this protein likely impairs the function of the complex. As a result, RhoA-GTPase signaling is turned on abnormally, weakening cellular junctions and increasing the permeability of blood vessel walls. The increased leakage into the brain can cause health problems such as headaches, seizures, and bleeding in the brain (cerebral hemorrhage) in some people with cerebral cavernous malformations.

Mutations in the *KRIT1* gene account for up to 50 percent of all familial cerebral cavernous malformation cases. One particular mutation is responsible for up to 70 percent of cases in people of Hispanic heritage. This mutation changes a single DNA building block (nucleotide) at position 1363 in the KRIT1 gene, written as 1363C>T.

Chromosomal Location

Cytogenetic Location: 7q21.2, which is the long (q) arm of chromosome 7 at position 21.2

Molecular Location: base pairs 92,198,969 to 92,246,128 on chromosome 7 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- ankyrin repeat-containing protein Krit1
- CAM
- CCM1
- cerebral cavernous malformations 1
- krev interaction trapped 1
- KRIT1_HUMAN

Additional Information & Resources

Educational Resources

- Madame Curie Bioscience Database (2000): Modulation of Barrier Function by Rho GTPases
<https://www.ncbi.nlm.nih.gov/books/NBK6487/#A36981>

GeneReviews

- Familial Cerebral Cavernous Malformation
<https://www.ncbi.nlm.nih.gov/books/NBK1293>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28CCM1%5BTIAB%5D%29+OR+%28cerebral+cavernous+malformations+1%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

OMIM

- KREV INTERACTION TRAPPED 1
<http://omim.org/entry/604214>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_KRIT1.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=KRIT1%5Bgene%5D>
- HGNC Gene Family: Ankyrin repeat domain containing
<http://www.genenames.org/cgi-bin/genefamilies/set/403>
- HGNC Gene Family: FERM domain containing
<http://www.genenames.org/cgi-bin/genefamilies/set/1293>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=1573
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/889>
- UniProt
<http://www.uniprot.org/uniprot/O00522>

Sources for This Summary

- Cavé-Riant F, Denier C, Labauge P, Cécillon M, Maciazek J, Joutel A, Laberge-Le Couteulx S, Tournier-Lasserre E. Spectrum and expression analysis of KRIT1 mutations in 121 consecutive and unrelated patients with Cerebral Cavernous Malformations. *Eur J Hum Genet.* 2002 Nov;10(11): 733-40.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12404106>
- Glading A, Han J, Stockton RA, Ginsberg MH. KRIT-1/CCM1 is a Rap1 effector that regulates endothelial cell cell junctions. *J Cell Biol.* 2007 Oct 22;179(2):247-54.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17954608>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2064761/>

- Gunel M, Laurans MS, Shin D, DiLuna ML, Voorhees J, Choate K, Nelson-Williams C, Lifton RP. KRIT1, a gene mutated in cerebral cavernous malformation, encodes a microtubule-associated protein. *Proc Natl Acad Sci U S A*. 2002 Aug 6;99(16):10677-82. Epub 2002 Jul 24.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12140362>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC125011/>
- Guzeloglu-Kayisli O, Kayisli UA, Amankulor NM, Voorhees JR, Gokce O, DiLuna ML, Laurans MS, Luleci G, Gunel M. Krev1 interaction trapped-1/cerebral cavernous malformation-1 protein expression during early angiogenesis. *J Neurosurg*. 2004 May;100(5 Suppl Pediatrics):481-7.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15287459>
- OMIM: KREV INTERACTION TRAPPED 1
<http://omim.org/entry/604214>
- Laberge-le Couteulx S, Jung HH, Labauge P, Houtteville JP, Lescoat C, Cecillon M, Marechal E, Joutel A, Bach JF, Tournier-Lasserre E. Truncating mutations in CCM1, encoding KRIT1, cause hereditary cavernous angiomas. *Nat Genet*. 1999 Oct;23(2):189-93.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/10508515>
- Plummer NW, Zawistowski JS, Marchuk DA. Genetics of cerebral cavernous malformations. *Curr Neurol Neurosci Rep*. 2005 Sep;5(5):391-6. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16131422>
- Stockton RA, Shenkar R, Awad IA, Ginsberg MH. Cerebral cavernous malformations proteins inhibit Rho kinase to stabilize vascular integrity. *J Exp Med*. 2010 Apr 12;207(4):881-96. doi: 10.1084/jem.20091258. Epub 2010 Mar 22.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20308363>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2856024/>
- Verlaan DJ, Davenport WJ, Stefan H, Sure U, Siegel AM, Rouleau GA. Cerebral cavernous malformations: mutations in Krit1. *Neurology*. 2002 Mar 26;58(6):853-7. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/11914398>
- Verlaan DJ, Laurent SB, Sure U, Bertalanffy H, Andermann E, Andermann F, Rouleau GA, Siegel AM. CCM1 mutation screen of sporadic cases with cerebral cavernous malformations. *Neurology*. 2004 Apr 13;62(7):1213-5.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15079030>
- Whitehead KJ, Plummer NW, Adams JA, Marchuk DA, Li DY. Ccm1 is required for arterial morphogenesis: implications for the etiology of human cavernous malformations. *Development*. 2004 Mar;131(6):1437-48.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/14993192>
- Zawistowski JS, Stalheim L, Uhlik MT, Abell AN, Ancrile BB, Johnson GL, Marchuk DA. CCM1 and CCM2 protein interactions in cell signaling: implications for cerebral cavernous malformations pathogenesis. *Hum Mol Genet*. 2005 Sep 1;14(17):2521-31. Epub 2005 Jul 21.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16037064>

Reprinted from Genetics Home Reference:
<https://ghr.nlm.nih.gov/gene/KRIT1>

Reviewed: November 2012
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services